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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/806,611	03/22/2004	Mary Collins	01997.043200.	2470

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EXAMINER	
WANG, CHANG YU	
ART UNIT	PAPER NUMBER
1649	
MAIL DATE	DELIVERY MODE
10/28/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/806,611	COLLINS ET AL.	
	Examiner	Art Unit	
	CHANG-YU WANG	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-15,19,29-36 and 50-73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-15, 19, 29-36 and 50-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/18/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RESPONSE TO AMENDMENT

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/20/09 & 8/18/09 has been entered.

Status of Application/Amendments/claims

2. Applicant's amendment filed 7/20/09 is acknowledged. Claims 2-3, 16-18, 20-28, and 37-49 are cancelled. Claims 1, 4-5, 9, 29-30, and 34-35 are amended. Claims 50-73 are newly added. Claims 1, 4-15, 19, 29-36, and newly added claims 50-73 are pending in this application and are under examination with respect to IFN-1α/β in this office action.

3. Any objection or rejection of record, which is not expressly repeated in this office action, has been overcome by Applicant's response.

4. Applicant's arguments filed on 7/20/09 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections/Objections Withdrawn

5. The rejection of claims 1,3-4, 9-12, 14 and 29-34 under 35 U.S.C. 102 (e) as being anticipated by Novak et al. (US Patent No. 6605272) is withdrawn in response to Applicant's amendment to the claims and Applicant's amendment of reciting a specific change for the IL-10 parameter and the IFN-γ parameter.

The rejection of claims 1,3-15,17-19, and 29-34 under 35 U.S.C. 103(a) as being unpatentable over Novak et al. (US Patent No. 6605272) in view of Carter et al. (US20030108549A) and Kawai et al. (Cell Immunol. 1996. 171:262-8)) is withdrawn in response to Applicant's amendment to the claims and Applicant's amendment of reciting a specific change for the IL-10 parameter and the IFN-γ parameter.

The rejection of claims 1,3-15,17-19,29-36 and 38-40 under 35 U.S.C. 103(a) as being unpatentable over Novak et al. (US Patent No. 6605272), Carter et al. (US20030108549A) and Kawai et al. (Cell Immunol. 1996. 171:262-8) and further in view of Beebe et al. (Cytokine & Growth Factor Rev. 2002. 13: 403-12) is withdrawn in response to Applicant's amendment to the claims and Applicant's amendment of reciting a specific change for the IL-10 parameter and the IFN-γ parameter.

Claim Rejections/Objections Maintained

In view of the amendment filed on 7/20/09, the following rejections are maintained.

Claim Objections

6. Claim 4 is objected to because it does not depend from a preceding claim. A series of singular dependent claims is permissible in which a dependent claim refers to a preceding claim which, in turn, refers to another preceding claim.

A claim which depends from a dependent claim should not be separated by any claim which does not also depend from said dependent claim. It should be kept in mind that a dependent claim may refer to any preceding independent claim. In general, applicant's sequence will not be changed. See MPEP § 608.01(n).

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-15, 19, 29-36 and 50-73 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for increasing production of IL-10 and decreasing INF-γ ,IL-1α, IL-2, IL-6, IL-18 and increasing T cell proliferation in an EAE animal model by administration of the IL-21 polypeptide of SEQ ID NO:2 to decrease the severity of symptoms in MS that are regulated by inappropriate cytokine production, does not reasonably provide enablement for decreasing an undefined INF-γ parameter in a subject having an undefined excess of INF-γ or for increasing an undefined IL-10 parameter in a subject having an undefined IL-10 deficiency by administering to the subject an agonist of an IL-21/IL-21R as recited in claims 1, 29, 34

and 35 as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The rejection is maintained for the reasons made of record and as follows.

Claims 1, 4-15, 19, 29-36 and 50-73 as amended are drawn to a method of decreasing an undefined INF-γ parameter in a subject having an excess of INF-γ or for increasing an undefined IL-10 parameter in a subject having an IL-10 deficiency by administering to the subject an agonist of an IL-21/IL-21R wherein the agonist is selected from the group consisting of a human IL-21 polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NOs: 2 or 4 or an agonistic anti-human/mouse IL-21R antibody or antigen binding fragment binding to an IL-21R comprising SEQ ID NOs: 6 or 8.

On p. 15 of the response, Applicant argues that the rejection has been overcome because independent claims have been amended to recite specific IL-21 polypeptides and the specification is enabled for increased production IL-10 and decreased IFN-γ. Applicant's arguments have been fully considered but they are not persuasive.

In contrast to Applicant's arguments, the specification fails to provide sufficient guidance to enable a skillsed artisan to practice the claimed invention commensurate in scope with the claims without undue experimentation. The instant specification only teaches patients with MS has an IL-10 deficiency and administration of IL-21 polypeptides (SEQ ID NO:2) can increase IL-10 production and also decrease the

production of other cytokines including IFN-γ. However, amended claims are not limited to the enabling method, which is directed to increasing production of IL-10 and decreasing INF-γ,IL-1α, IL-2, IL-6, IL-18 ,and increasing T cell proliferation in an EAE animal model by administration of the IL-21 polypeptide of SEQ ID NO:2 to decrease the severity of symptoms in MS that is regulated by inappropriate cytokine production.

Instant claims 1, 4-15, 29-33, 50-53 now encompass a undefined subject having an excess of IFN-γ and undefined IFN-γ parameters. The instnat specification fails to teach what a subject having an excess of IFN-γ is and thus can be treated in the claimed method. The specification also fails to establish a common correlation between MS that is regulated by inappropriate cytokine production and other diseases. Thus, it is unpredictable what other diseases would have an excess of IFN-γ. The specifiation also fails to teach what an IFN-γ parameter is. The specification provide no guidance as to how to use or measure IFN-r parameter because the IFN-r parameter is undefined. Thus, a skilled artisan cannot contemplate how to use the claimed invention. The specification fails to provide sufficient guidance to enable a skilled artisan to use an unknown parameter (undefined INF-γ parameters) to evaulate or to determine an unknown disease (an undefined subject having an excess of IFN-γ). Note that the scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, it is unpredictable what parameters, activities of IL-10 or IFN-γ can be measured and what subjects can be treated. Thus, the experimentation left to those skilled in the art is extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986). Thus, the skilled

artisan cannot readily make and use the claimed invention as currently claimed without further undue experimentation. Note that

"The 'predictability or lack thereof' in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Accordingly, what is known in the art provides evidence as to the question of predictability. In particular, the court in In re Marzocchi, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971)" See MPEP § 2164.03.

In addition, instant claims 34-36 and 54-73 are directed to increasing an IL-10 parameter in a subject having IL-10 deficiency. The specification fails to teach what an IL-10 parameter is. Note that the specification only teaches that patients with MS, ischemia-reperfusion injury, psoriasis and pemphingus (see p. 8, [0026]) would have an IL-10 deficiency. However, the specification fails to teach what other diseases would have an IL-10 deficiency and would have common characteristics for patients as set forth above, and thus can be treated in the claimed methods. Furthermore, the specification only describes examples to assay or evaluate an IL-10 activity but fails to limit what other specific number or parameters and activity of IL-10 and IFN-γ are and would be within the scope of the claims to be used in the claimed method to evaluate and determine the effects. Note that a patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentec, Inc, v. Novo Nordisk*, 42 USPQ 2d 100,(CAFC 1997), the court held that:

"[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue

experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The instant specification is not enabling because one can not follow the guidance presented therein and practice the claimed method without first making a substantial inventive contribution.

8. Claims 1, 4-15, 19, 29-36 and 50-73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is maintained for the reasons made of record.

Claims 1, 4-15, 19, 29-36 and 50-73 as amended are drawn to a method of decreasing an undefined INF-γ parameter in a subject having an excess of INF-γ or for increasing an undefined IL-10 parameter in a subject having an IL-10 deficiency by administering to the subject an agonist of an IL-21/IL-21R wherein the agonist is selected from the group consisting of a human IL-21 polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NOs: 2 or 4 or an agonistic anti-human/mouse IL-21R antibody or antigen binding fragment binding to an IL-21R comprising SEQ ID NOs: 6 or 8.

On p. 15 of the response, Applicant argues that the rejection has been overcome because independent claims have been amended to recite specific IL-21 polypeptides having specific sequences and agonistic anti-human IL-21R antibodies. Applicant's arguments have been fully considered but they are not persuasive.

In response, although amended claims have overcome the written description rejection due to the limitation of IL-21 polypeptides and antibodies, newly amended claims also encompass a genus of IFN-γ parameters, a genus of a subject having an excess of IFN-γ, a genus of IL-10 parameters and a genus of a subject having an IL-10 deficiency. The specification only teaches that patients with MS, ischemia-reperfusion injury, psoriasis and pemphingus (see p. 8, [0026]) would have an IL-10 deficiency but fails to teach what other diseases would have an IL-10 deficiency and would have common characteristics for patients as set forth above and thus can be treated in the claimed methods. In addition, the specification fails to define what a subject having an excess of IFN-γ is and thus can be treated in the claimed method.

Furthermore, the specification only describes examples to assay or evaluate IL-10 activity but fails to limit what specific number or parameter of IL-10 and IFN-γ are. Thus,the instant specification fails to provide sufficient information to demonstrate that Applicant was not reasonably in possession of the claimed genus of subjects with an excess of IFN-g and a genus of subjects with an IL-10 deficiency" to be treated in the claimed methods. Moreover, the specification also fails to reasonably demonstrate that Applicant was in possesion of the claimed genus of IFN-γ parameters and the claimed genus of IL-10 parameters to be used in the claimed methods.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-15, 19, 29-35, 51-52, 54-57 and 59-73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is maintained for the reasons made of record and as follows.

On p. 16 of the response, Applicant argues that the rejection is overcome because independent claims 1, 29, 34 and 35 to include a specific quantity by which to evaluate the IL-10 and IFN-γ parameter. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, as previously made of record, the specification only describes examples to assay or evaluate IL-10 activity but fails to limit what specific number or parameter of IL-10 and IFN-γ are. Note that there are two separate requirements set forth in this 112-2nd paragraph: (A) the claims must set forth the subject matter that applicants regard as their invention; and (B) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant. In this case, it is unclear to a skilled artisan what numbers, parameters , expression levels or any biological activity of IL-10 and IFN-γ are within the scope of the claims and thereby to be used to measure and determine the efficacy of the treatment.

According, the metes and bounds of the definitation of the IFN-γ and IL-10 parameter cannot be determined and thus the claims are indefinite.

New Grounds of Rejection Necessitated by the Amendment

The following rejections are new grounds of rejections necessitated by the amendment filed on 7/20/09.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-15, 19 and 29-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 1, 4-15, 19 and 29-33 as amended are drawn to a method of decreasing an undefined INF-γ parameter in a subject having an excess of INF-γ by administering to the subject an agonist of an IL-21/IL-21R wherein the agonist is selected from the group consisting of a human IL-21 polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NOs: 2 or 4 or an agonistic

anti-human/mouse IL-21R antibody or antigen binding fragment binding to an IL-21R comprising SEQ ID NOs: 6 or 8.

The instant claims now recite the limitation of “decreasing IFN-γ parameter in a subject having an excess of IFN-γ” and the limitation of “wherein the IFN-γ parameter of the subject having the excess IFN-γ is decreased at least 2 fold" in independent claims 1 and 29, which were not clearly disclosed in the specification and claims as filed, and now change the scope of the instant disclosure as filed.

On p. 14 of the response, Applicant states that support for the amendments and newly added claims can be found at p. 5, [0014]; p. 8, [0025]; p. 13, [0048] to p. 14, [0050]; p. 50, [0181]; tables 2 and 4. However, no such support for the new limitations was found in the recited pages and paragraphs. The new limitations were not in the specification or original claims, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

The specification only teaches “a decrease in an IFN-γ parameter to .....". However, the specification fails to disclose the limitation of “a subject having an excess of IFN-γ”. Accordingly, in the absence of sufficient recitation of “a subject having an excess of IFN-γ”, the specification does not provide adequate written description to support the new limitation as recited in instant claims 1 and 29. Support is not found for the new limitation as disclosed in the original specification and thus the recitation constitutes new matter absent evidence for their support. Applicant is required to cancel the new matter in the reply to this office action. Alternatively, Applicant is invited to clearly point out the written support for the instant limitations.

Conclusion

11. NO CLAIM IS ALLOWED.

12. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chang-Yu Wang, Ph.D.
October 15, 2009

/Chang-Yu Wang/
Examiner, Art Unit 1649